In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-1511V

(Not to be published)

ROBIN LARA CAMACHO KEJA,	*	
	*	Chief Special Master Corcoran
Petitioner,	*	
	*	Filed: April 2, 2021
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Charles W. Marsar, R.J. Marzella & Associates, P.C., Harrisburg, PA, for Petitioner

Ryan Daniel Pyles, U.S. Dep't of Justice, Washington, DC, for Respondent

ENTITLEMENT DECISION[1]

On October 13, 2017, Robin Lara Camacho Keja filed a petition seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program")[2] alleging that the influenza ("flu") vaccine that she received on October 17, 2014, caused her to develop a number of injuries, "including Lupus, inflammatory arthritis, Serum-like Sickness, and Prurigo

[1] Although not formally designated for publication, this Decision will nevertheless be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

Nodularis." *See* Petition ("Pet.") at 1.[3]

The parties have agreed that the matter could best be resolved on the papers. Accordingly, on September 30, 2020, Petitioner filed a motion requesting that the Court find entitlement in her favor. Motion, filed Sept. 30, 2020 (ECF No. 43), and Brief in Support, filed Sept. 30, 2020 (ECF No. 44) ("Mot."). On November 30, 2020, Respondent filed a Response and Cross-Motion for Ruling on the Record dismissing the claim. *See* Resp.'s Motion, filed Nov. 30, 2020, (ECF No. 47) ("Opp."). Petitioner elected not file a response.

Because Petitioner was never diagnosed with the injuries she claims to have been vaccine caused, and her expert's theory was not persuasive and/or unsupported by other reliable evidence, I hereby deny entitlement in this matter.

I. Medical History

Relevant Pre-Vaccination Events

Certain health problems Ms. Camacho Keja experienced pre-vaccination echo the injuries alleged in this case. In particular, her medical history includes both issues with her lymph nodes as well as rheumatologic-like symptoms.

On September 28, 2010, for example, Petitioner saw otolaryngologist Andrew Shorb, M.D., following a lymph node biopsy the week prior that was benign, "consistent with a reactive lymph node." Ex. 18 at 17. Due to her continuing "generalized sense of fatigue and lethargy," however, Dr. Shorb recommended a rheumatology consultation, noting that she had seen a rheumatologist "in the past." *Id.* Almost two years later, on January 29, 2012, Petitioner was seen by her primary care physician for acute bronchitis. Ex. 11 at 17. At that time, her "active problems" included localized joint pain in more than one joint, exercise-induced asthma, nephrolithiasis (kidney stones), dysmenorrhea, and "[p]arvovirus B19 [a]rthritis." *Id.* Later that month, while she was twenty-eight weeks pregnant, Petitioner had multiple joint effusions. *Id.* at 8.

On January 20, 2013, Petitioner was seen by Todd Curran, D.O., for an orthopedic evaluation regarding left-sided neck pain and shoulder pain, which she characterized as chronic, although the pain had worsened over the prior week. Ex. 2 at 262. She also reported occasional numbness of her hands bilaterally (worse on the left side). *Id.* Dr. Curran's impression was left shoulder pain, "[p]arascapular trigger points," and rotator cuff tendonitis, and he administered a steroid injection to Petitioner. *Id.* at 263-64.

On October 26, 2013, Ms. Camacho Keja was prescribed prednisone by Certified Nurse

[3] This case was originally assigned to former Special Master Millman, then transferred to Special Master Horner upon her retirement in 2019. It was transferred a second time, to me, on July 29, 2020. *See* ECF Nos. 40-41.

Midwife (CNM) Deborah Brown at WellSpan Health, Women and Children Services. Ex. 41 at 2; Ex. 45 at 16. Petitioner has alleged that two days later (October 28, 2013) she received a flu vaccine.[4] Ex. 10 at 1. There are no records in the five weeks thereafter of any reaction, however. At best, on December 6, 2013, Petitioner was seen at her primary care doctor for a "solitary skin lesion" located on her chin of a several-week duration, but she denied the presence of any "arthralgias, fever, headache, myalgias, sore throat and rash." Ex. 2 at 38. At most, treaters noted a left submandibular node on examination, and assessed her with acute lymphadenitis to be treated with Augmentin, an antibiotic. *Id.* at 39-40.

Later that same month, on December 17, 2013, Ms. Camacho Keja was seen for acute swelling of "submental" (meaning the area of the head below the chin and around the neck) lymph nodes. Ex. 2 at 101. She reported that about two days prior to the acute swelling, she had a sore throat that "never developed into a significant upper respiratory infection," and that she had "noticed a significant reduction in size of the nodule" after taking Augmentin. *Id.* She reported no other head or neck symptoms at this time, and the assessment was swelling in the head and neck and lymph node enlargement. *Id.* During a follow-up visit on January 9, 2014, following a course of Augmentin and "some prednisone," Petitioner now informed treaters that she had "noticed a dramatic reduction [in swelling of the submental node] and [was] without other complaints or symptoms." *Id.* at 103.

On February 7, 2014, Ms. Camacho Keja went to the emergency room reporting a six-day history of "subjective fevers, fatigue, myalgias, nausea[,] vomiting, [and] mild intermittent diarrhea." Ex. 2 at 55. She also complained of "mild to intermittent left lower quadrant abdominal pain," and reported that she had been taking Tamiflu following a telephone prescription from her primary care physician. *Id.* Petitioner denied chest pain, shortness of breath, leg swelling, or rashes. *Id.* The differential diagnoses were fever, viral syndrome, and gastroenteritis. *Id.* at 56. At a follow-up visit on February 18, 2014, Petitioner was assessed with a cough, and the treater noted a suspicion of bronchitis. *Id.* at 37. On April 11, 2014, Ms. Camacho Keja filled a prednisone prescription from Deborah Brown, CNM. Ex. 45 at 16. No accompanying records filed in the matter explain the reason for the prescription.

Vaccination and Subsequent History

On October 17, 2014, Petitioner received the flu vaccine at issue in this case from her employer. *See* Ex. 1. Four days later, on October 21, 2014, Ms. Camacho Keja saw a primary care doctor, Nandita Kinley, M.D., with the following history:

[4] Although in subsequent records Ms. Camacho Keja reported to treaters that she received a flu vaccine at this time, proof of vaccination was not filed. Petitioner filed an affidavit dated November 19, 2018, in which she stated that she could not recall where the alleged vaccination occurred, although she believes it may have been at York Hospital (WellSpan), where she was employed at the time. Ex 38 at 1–2.

> "Patient complains of lymph node enlargement. A possible swollen lymph node that was first noticed yesterday. This is located in the left upper neck. The lymph node is characterized as tender, firm, mobile, and enlarging in size. Related symptoms include **localized swelling**, but not earache, fever, nervousness, rash, systemic fever, toothache. [Patient] was here last week. A few days after having received her flu vaccine, she had some "generalized lymphandenopathy." Her[e] now about the constellation of [symptoms] that have been ongoing for the last 6 mo[nths] at least and also with this new [lymph node]. She did have a major work up years ago and a lymphnode [sic] excision. [Workup] was negative at that time. [Patient] is now a single mom with a lot of stressors. She is afraid there is something terribly wrong going on."

Ex. 2 at 31 (emphasis in original). The plan and assessment following this appointment included lymphadenopathy, rash, and diffuse arthralgia, and multiple diagnostic tests were ordered. *Id.*

A week later, on October 28, 2014, Ms. Camacho Keja was seen at Wellspan Ready Care and reported gaining eleven and a half pounds in a week, and also that she was now experiencing a pitting edema that was worse than when she was seen the previous day in primary care. Ex. 2 at 104. Petitioner reported being treated with prednisone the previous week for an allergic reaction to her vaccination. *Id.* On November 4, 2014, Petitioner presented to primary care with complaints of edema. *Id.* at 28. At the time of this appointment, Petitioner's swelling was represented to have been present for several weeks and primarily involved her lower extremities. *Id.* On exam, her physician noted Petitioner was anxious, had 1+ pedal edema, and a firm non-tender lymph node. *Id.* at 30.

On December 3, 2014, Ms. Camacho Keja again presented to primary care with complaints of feet and ankle swelling. Ex. 2 at 25. During this appointment the treating physician, Dr. Nandita Kinley, notes: "[t]he question is, was there an inciting event that promoted this? [Patient] had similar [symptoms] last [year] about 1 w[ee]k after flu administration. This year, she's had the same [symptoms] and more, but to a worse degree. Could this be a strange, delayed allergic [reaction] to flu? Could something autoimmune be going on?" *Id.* at 27. On exam, only "trace pedal edema" was noted. *Id.* at 30. Petitioner was referred to rheumatology, allergy/immunology, and dermatology. *Id.*

The next day (December 4th), Petitioner visited the Family Center for Allergy and Asthma in York, Pennsylvania for further evaluation of her on-going symptoms. Ex. 2 at 106. She reported at this appointment that after receiving the flu vaccine the year prior (2013), she suffered facial swelling, a sense of fullness, and itching of her neck, all of which resolved following a course of Prednisone. *Id.*; Ex. 40 at 2. In response, the doctor at this appointment noted her assessment as

"[a]ngioedema, fluid retention, reactive lymph node, in the aftermath of receiving the seasonal flu vaccine[.]" Ex. 2 at 108. In addition, the attending physician deemed the circumstances to present "a very complicated case. It [] certainly seems that she has some kind of underlying inflammatory condition that may have predisposed her reaction to the influenza vaccine." *Id.*

On December 23, 2014, Ms. Camacho Keja presented to Sadia Kahn, M.D., a rheumatologist, for a consultation. Ex. 2 at 111. Dr. Khan noted in part the following:

> I had seen [Petitioner] previously in 2010 when she had enlarged lymph nodes in cervical region and excision biopsy showed reactive process. I do not find evidence of autoimmune disease. She had mild elevation of CRP 0.86. She reports that she was in her usual state of health until October when she received flu vaccination this year. She developed facial swelling 24 hours after taking flu vaccine. She also started to notice trouble swallowing smaller pills. She noticed lower extremity edema. She felt stiff. She had similar reaction a year prior from flu vaccination. Within few hours she developed tingling along left side of her jaw. She also developed itching in the arm pits and neck area. She felt that her lymph nodes were enlarged. She was seen by PCP [primary care physician]. She was started on prednisone 40 mg daily with gradual taper. However if [sic] she then developed worsening edema… She reports that symptoms lasted for about one to two weeks and have resolved now…

Ex. 2 at 111 (*see also* Ex. 7 at 7 (same)). On December 29, 2014, Petitioner saw her primary care provider for a cough and/or an acute infection (questioned to be either bronchitis or pneumonia). Ex. 2 at 22-23. On January 7, 2015, Petitioner saw her primary provider for an acute cough and four weeks of acute illness, including chest congestion, shortness of breath, body aches, headaches, nasal congestion, chills, and malaise. *Id.* at 19.

On February 2, 2015, Ms. Camacho Keja presented to primary care due to concerns of kidney stones and other ailments. Ex. 2 at 15. The assessment included pedal edema, and her treater decided to stop Petitioner's over-the-counter prescriptions in order to ascertain whether any medications were exacerbating what could be an ongoing inflammatory condition. *Id.* at 16. On February 10, 2015, Petitioner presented to Family Center for Allergy and Asthma for a follow-up visit. *Id.* at 126. The record notes that Petitioner's ankles were asymmetrical, possibly suggestive of swelling. *Id.* The assessment indicated a "[c]oncern for angioedema, fluid retention, reactive lymph node in the aftermath of receiving the seasonal flu vaccine, [and] possible serum sickness." *Id.*

On April 15, 2015, Ms. Camacho Keja returned to her primary care physician with edema. Ex. 2 at 9. Treaters indicated a plan to repeat blood work and to refer to rheumatology. *Id.* On

April 28, 2015, Petitioner visited WellSpan Rheumatology. *Id.* at 162. Treaters explained that Petitioner lacked the diagnostic criteria that would suggest the existence of an autoimmune rheumatic process, but that she did have some laboratory abnormalities that did not fit into a clear diagnostic category. *Id.* A musculoskeletal exam also showed "[m]ild diffuse tenderness to palpitation of both ankles… [m]ild tenderness to palpitation of MTP joints without obvious joint effusions." *Id.*

Several months later, on August 4, 2015, Ms. Camacho Keja presented to Hershey Medical Center ("HMC") Rheumatology for a second opinion. Ex. 2 at 200. Treater Sowmya Surapaneni, M.D., expressed concern regarding whether the ongoing symptoms were indicative of serum sickness. *Id.* at 202. Dr. Surapaneni ordered extensive lab tests to rule out any underling autoimmune disease. *Id*. Specifically, Dr. Surapaneni ordered a Serum Protein Electrophonesis Interpretation, which revealed "[n]ormal serum protein with polyclonal distribution in the gamma region. Serum total protein and albumin within reference limits. No evidence of monoclonal immunoglobulin is present." *Id*.

On November 24, 2015, Ms. Camacho Keja again presented to primary care with ankle and feet swelling. Ex. 2 at 2. The next year, on February 2, 2016, Petitioner returned to HMC Rheumatology to see Dr. Surapaneni for a follow up. *Id.* 246. The record from this visit notes that Petitioner's left knee appeared slightly swollen and warm when compared to her right knee. *Id.* at 247. Two days later, on February 4, 2016, Petitioner was seen in the HMC Allergy and Immunology Clinic by Faoud Ishmael, M.D., who noted that Petitioner's facial swelling appeared "only directly after [her] flu vaccines, but she continued to have lots of peripheral swelling." *Id.* at 242.

On February 9, 2016, Dr. Ishmael provided a message to Ms. Camacho Keja, stating: "my overall feeling is that you had an underlying autoimmune disease that was brewing… and that it was more the overall stimulation of the immune system from the vaccine that set this all in motion." Ex. 3 at 253. In addition, Dr. Ishmael wrote that "we do see a lot of cases where patients… have flares of lupus after an infection or an immunization, and that in those cases the 'turning on' of the immune system is what sets things off." *Id.*

On June 16, 2016, Ms. Camacho Keja returned to HMC Rheumatology for a follow-up with Dr. Surapaneni. Ex. 2 at 256. Dr. Surapaneni noted that "[t]here is no obvious swelling that [he] could notice in the knees today, but there is pain with range of movements around both knees. *Id.* at 257. He also noted that the "[l]eft ankle seems subtly swollen when compared to the right, but this is better than what I have seen before… MTPs, especially the left MTPs are tender." *Id.*

Almost a year later, on April 18, 2017, Ms. Camacho Keja saw Dr. Surapaneni for another follow-up for her "inflammatory arthritis." Ex 3 at 53. Dr. Surapaneni noted that "[a]t this point,

[he] is starting to wonder if the inflammatory arthritis [Petitioner] has is related to some form of underlying spondyloarthropathy…" *Id.* In addition, he recorded that Petitioner reported "more swelling and pain[,] especially in the knees, ankles, and left hip associated with stiffness in the mornings…" *Id.* With regard to prior lab testing, Dr. Surapaneni noted:

> [T]he blood work in the past has shown ANA to be negative including DNA Smith, RNP, SSA, SSB, centromere, scleroderma, histo and Jo-1 antibodies which were all negative. CRP and sed[imentation] rate were elevated back in February of 2016, but the repeat [labs] from June 2016 were within normal limits. Ultrasound of her ankles from November has shown diffuse nonspecific subcutaneous edema about the ankles with no evidence of inflammatory arthritis at which point, we did lymphoscintigraphy imaging on TOMO [on January 3, 2017 (Ex. 3 at 85)] which did not show any abnormal lymphatic drainage.

Ex. 3 at 53. On October 3, 2017, Ms. Camacho Keja presented to urgent care for left wrist pain, bilateral knee pain, and bilateral ankle pain that lasted for a day, specifically after falling down and rolling her right ankle. Ex. 12 at 1. Petitioner also reported during this visit that while walking into her garage, "her knees gave out, causing her to fall and roll her right ankle. She remembers catching herself with her hands and landing on her right side." *Id.* No medical records after the fall of 2017 (other than pharmacy records up to 2018) were filed in this case.

II. Expert Reports

A. *Dr. Thomas M. Zizic*

Dr. Zizic's expert report was the sole opinion filed on Petitioner's behalf. Report, dated September 21, 2018, filed as Ex. 20 (ECF No. 26) ("Zizic Rep."). Dr. Zizic maintains that Petitioner likely developed spondyloarthropathy, a kind of inflammatory arthritis, as a result of her receipt of the flu vaccine. Zizic Rep. at 21.

Dr. Zizic is a physician and Associate Professor of Medicine at Johns Hopkins Hospital and Johns Hopkins University School of Medicine in Baltimore, Maryland. *See* CV, filed as Ex. 21 (ECF No. 27) at 1. He received his medical degree from Johns Hopkins University School of Medicine and served an internship and residency at John Hopkins University Hospital Center in internal medicine. *Id.* Previously, Dr. Zizic was the Associate Director of the Rheumatic Disease Unit for John Hopkins at the Good Samaritan Hospital. Zizic Rep. at 1. Dr. Zizic is a former President of the Maryland Society of Rheumatic Disease and served on the National Committees of the Arthritis Foundation and the Lupus Foundation. *Id.* at 2. Dr. Zizic has published approximately 100 articles and abstracts in peer reviewed journals as well as several dozen chapters in textbooks of medicine. *Id.* He has also conducted clinical research studies. *Id.*

Dr. Zizic opined that there is a cause-effect relationship between Petitioner's receipt of the flu vaccine and her subsequent development of an inflammatory arthritis, since "current scientific knowledge delineates a highly plausible biologic mechanism for vaccination induced autoinflammatory diseases" in susceptible individuals. Zizic Rep. at 15. As possible specific mechanisms for such a process, Dr. Zizic described three means of autoimmune recognition of the innate immune system: (1) the "microbial non-self;" (2) the recognition of "missing self;" and (3) recognition of "induced or altered self." *Id.* Any one of these three responses, he maintained, could have been activated by the flu vaccine. *Id.*

As Dr. Zizic generally explained, autoimmune diseases are characterized by reactivity to self-antigens, leading to chronic inflammation. Zizic Rep. at 16. The basis for the first kind of autoimmune response, microbial non-self recognition, lies in the ability of the host to recognize conserved products of microbial metabolism that are unique to microorganisms and are not produced by the host. Zizic Rep. at 15. The second, recognition of "missing self," involves detection of markers of normal self, coupled with various inhibitory pathways that block initiation of autoimmune responses. *Id.* These markers (MHC molecules)[5] are commonly expressed on cell surfaces, but can be down-regulated in an infectious process, leading the body's innate immune system to mistake healthy cells for infected, indiscriminately attacking both. *Id.* And the third, recognition of induced self, is based on the detection of markers of abnormal self that are induced upon infection and cellular transformation. *Id.* These markers tag affected cells for elimination by the immune system. *Id.*

Autoimmune diseases, Dr. Zizic maintained, are characterized by "unchecked T-cell and/or B-cell reactivity to self-antigens, leading to chronic inflammation." Zizic Rep. at 16.[6] Certain prototypical autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus, also share a number of common features such as genetic risk factors, marked female predominance, an association with disease-specific autoantibodies, and a positive response to T-cell or B-cell targeted treatments (thus underscoring their autoimmune character). *Id.*

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[5] The "major histocompatibility complex" ("MHC") is a group of genes in mammals that code for cell-surface polymorphic glycoprotein molecules which display antigenic peptide fragments for T cell recognition, thereby aiding in the ability of the immune system to differentiate self from non-self. Merriam-Webster's Online Dictionary, https://www.merriam-webster.com/dictionary/major%20histocompatibility%20complex (last visited March 18, 2021).

[6] In a properly-functioning immune response, T cells coordinate defenses against pathogens by recognizing pathogen-derived peptides and producing immune-stimulatory hormones (cytokines) to activate cells of the immune system, and thereby control inflammation and suppress aberrant immune responses. Zizic Rep. at 16, *citing* P. Wright et al., *Dendritic Cells and Regulatory T cells in Spondyloarthritis*, 25(4) Current Opinion Rheumatology 440-447 (2013), filed as Ex 25 on Sept. 24, 2018 (ECF No. 29-3) ("Wright").

Dr. Zizic next discussed his proposed diagnosis for Petitioner's constellation of symptoms. Spondyloarthritis, he stated, is a polygenic immune-mediated inflammatory disease characterized by inflammation of the spine and peripheral joints, as well as extra-articular manifestations such as inflammatory bowel disease, uveitis, and psoriasis. Zizic Rep. at 19. Ankylosing spondylitis ("AS"), a spondylarthritis variant, is characterized by inflammation of the sacroiliac joints, peripheral inflammatory arthropathy, and the absence of rheumatoid factor. *Id.* Polymorphisms in ERAP1 and ERAP2[7] could, in Dr. Zizic's estimation, also be involved in the pathogenesis of the autoimmune process resulting in a spondyloarthritic condition, through alterations in peptide processing. Zizic Rep. at 20.

Finally, Dr. Zizic provided an opinion for how the flu vaccine could stimulate an autoimmune process resulting in a spondyloarthritis. As he hypothesized, viral proteins present in the vaccine could cause abnormal alterations in peptide processing, contributing to disease pathogenesis. In support of this contention, Dr. Zizic referenced a Toronto study in which the immune response to the influenza wild virus showed a change in the overall flu-peptide repertoire in mice deficient in ERAP function. Zizic Rep. at 20 (citing F. Tsui et al., *The Genetic Basis of Ankylosing Spondylitis: New Insights into Disease Pathogenesis*, 7 Application of Clinical Genetics 105-115 (2014), filed as Ex. 29 on Sept. 24, 2018 (ECF No. 29-7) ("Tsui"). Tsui did not involve the flu vaccine however, and no other literature was offered extending its findings to vaccination. Zizic nevertheless concluded that it is biologically plausible that the flu vaccine could (in a genetically susceptible host also possessing the relevant ERAP1 and/or ERAP2 mutations) cause a similar altered peptide processing with the generation of arthritogenic peptides, resulting in SA. Zizic Rep. at 20.

Dr. Zizic offered some literature specific to the alleged association between the flu vaccine and Petitioner's purported injury, although the items provided were of limited probative value. For example, Dr. Zizic referenced a case report from 1994 (presented in the form of a letter to the editor) to suggest that the flu vaccine has been shown to cause reactive arthritis. Zizic Rep. at 21 (citing D. Biasi et al., *A case of reactive arthritis after influenza vaccination* 13 Clinical Rheumatology 645 (1994), filed as Ex. 35 on Sept. 24, 2018 (ECF No. 29-13). But reactive arthritis is not alleged as the injury herein, and the record would not support it even if it had been. Dr. Zizic similarly provided a 2005 case report in which a patient developed a case of reactive arthritis after flu vaccination *Id.* at 21. (citing J. Asakawa et al., *Reactive arthritis after influenza vaccination: report of a case,* 15:4 Clinical Rheumatology 283-285 (2005), filed as Ex. 36 (ECF No. 29-14)

[7] ERAP1, or "Endoplasmic reticulum aminopeptidase 1," is a protein which plays a central role in peptide trimming, a step required for most HLA class I-binding peptides. *See* UniProt Consortium, UniProtKB - Q9NZ08 (ERAP1_HUMAN), available at https://www.uniprot.org/uniprot/Q9NZ08 (last visited March 18, 2021). Peptide trimming is essential to customize longer precursor peptides to fit them to the correct length required for presentation on MHC class I molecules. *Id.* The main function of the ERAP1 is to trim peptides within the ER (endoplasmic reticulum) into the right length. Zizic Rep. at 20. Malfunction of ERAP1 can lead to generation of anomalous peptides of incorrect length and sequence, which can result in misfolding (and thereafter produce aberrant downstream outcomes). *Id.*

("Asakawa"). However (and in addition to the fact that the injury is different), the subject in this report was found positive for a gene variant associated with AS (discussed in more detail below) that Ms. Camacho Keja herself has not been shown to possess. Asakawa at 283.

B. *Dr. Carlos D. Rose*

Dr. Rose, a board-certified rheumatologist, prepared one report for Respondent. Report, dated March 14, 2019, filed as Ex. A (ECF No. 33-1) ("Rose Rep."). Dr. Rose was asked to provide an opinion on the alleged effect of the flu vaccine on Petitioner's health, and also to respond to Dr. Zizic. Rose Rep. at 1, at 24-28. He disputed that Petitioner's vaccination impacted her health as alleged, and maintained that Petitioner's medical record did not support a finding that she more likely than not suffered from any definable rheumatic disease. *Id.* at 28.

Dr. Rose obtained his medical degree from the University of Buenos Aires School of Medicine and received a Fellows Research Award from American College of Rheumatology. Ex. B at 4. Dr. Rose also completed a specialty fellowship in Pediatric Rheumatology at Children's Hospital of Philadelphia and the Alfred I. du Pont Institute in Wilmington, Delaware. *Id.* He served as Professor of Pediatrics at Jefferson Medical College and Instructor of Pediatrics at University of Pennsylvania School of Medicine. *Id.* Currently, Dr. Rose serves on various medical committees and has been caring for adult and pediatric patients with rheumatic and autoimmune diseases since 1983. *Id.*; Rose Rep. at 1.

Dr. Rose began his report with an analysis of the contemporary medical records, starting on October 10, 2014 (four days after Petitioner's vaccination). *See generally* Rose Rep. In his view, the two inflammatory rashes Petitioner suffered from that puzzled some doctors have no relationship with any underlying autoimmune or rheumatic disorder. *Id.* at 9. He based this conclusion on the fact that, as the record reveals, Petitioner suffered from one kind of rash, diagnosed as Prurigo nodularis, DSAP (Disseminated superficial actinic porokeratosis, PLEVA (Pytyriasis lichenoides varioliformis acuta) and sarcoidosis, since childhood. *Id.* The second rash, located on the sole of the right foot and present for two years as of 2014, was diagnosed as bullous tinea pedis (fungal infection), and as such could not be vaccine-caused. He therefore deemed this evidence as not indicative of a vaccine reaction.

Dr. Rose then analyzed relevant past medical records. As he noted, Petitioner's medical history pre-vaccination revealed numerous concerns regarding her lymph nodes. Rose Rep. at 10. In August of 2010, for example, Petitioner was seen for submental swelling since April of that year, with worsening over the prior one and one-half weeks, plus fatigue and dizziness. Ex. 18 at 32. A biopsy was performed at this time, however, and a later follow-up by treaters revealed a benign pathology consistent with a reactive lymph node, rather than a specific immunophenotypic abnormality. *Id.* at 18.

Data from the clinical evaluation of Petitioner's health post-vaccination was similarly, in Dr. Rose's view, unsupportive of Petitioner's claim. Rose Rep. at 12. Petitioner was seen at Wellspan Rheumatology in 2015, but physical examinations remained unrevealing, with treaters documenting the absence of joint inflammation (synovitis) and providing an assessment that once again ruled out rheumatic or autoimmune disease. Ex. 7 at 6. Later in 2015, a CT scan of Petitioner's abdomen and pelvis showed no abnormalities. Ex. 2 at 99-100. This finding was particularly notable to Dr. Rose, because it revealed no changes to the osseous structures, meaning that there was no fluid in the hip or involvement of the sacroiliac joints at this time—findings that would be consistent with Petitioner's alleged injury but which were (again) absent in the record. Rose Rep. at 15.

Dr. Rose then addressed Petitioner's self-reported claims to treaters of prednisone responsiveness. Rose Rep. at 15-16. Prednisone is a synthetic glucocorticoid derived from cortisone, administered orally as an anti-inflammatory and immunosuppressant in a wide variety of disorders. *Dorland's Medical Dictionary Online*, https://www.dorlandsonline.com/dorland/definition?id=40742&searchterm=prednisone (last visited January 26, 2020). According to pharmacy records filed in this case, Petitioner had only two prescriptions for prednisone, both very short in duration and occurring in 2013 and 2014. *See* Ex. 41; Ex. 45. Accordingly, unless pharmacy records filed in this case were incomplete, it was not in Dr. Rose's view possible to confirm Petitioner's claim of prednisone responsiveness, since her access to this medication had not been substantiated.

Dr. Rose also highlighted the mismatch between the evidence of symptoms in the record and Petitioner's proposed diagnoses. Rose Rep. at 17. Records contemporary to the 2014 vaccination, plus those around the time of the purported 2013 vaccination, suggest no diagnosable rheumatic or autoimmune disease associated with the symptoms recorded at the relevant times. *Id.* The totality of Petitioner's conditions described in late 2014 and early 2015 included fatigue, cervical lymphadenitis, hypertension, variable degrees of lower extremity edema, joint pain, skin rash, and slight elevation of inflammatory makers which were either long pre-existing or not specifically suggestive of a rheumatic or autoimmune disease. *Id.* at 17-18. Fatigue, Dr. Rose explains, can be caused by a multitude of factors including sleep deprivation, stress, mood disorders, long work days, deconditioning, and inflammatory or malignant diseases among other things. *Id.* at 18. And the record suggested it had been a prior issue for Petitioner, and not associated with a possible autoimmune rheumatic condition. *Id.*[8]

[8] According to the medical record, fatigue was documented as early as 2010 by Dr. Shorb as well as stress and fear, which were repeatedly noted in the record in 2014 as ongoing for six months. Rose Rep. at 18. Petitioner reported being under a lot of stressors as a single mother. *Id.* Dr. Kahn, the first rheumatologist who evaluated Petitioner in 2014, was consulted specifically to address persistent fatigue as part of a worker's compensation filing and he did not attribute Petitioner's symptoms to an autoimmune or rheumatic disorder. *Id.*

Cervical adenitis was also a recurrent problem for Petitioner, but it similarly preceded her post-vaccination symptoms. Rose Rep. at 18. And lower extremity edema, which was a confusing symptom to many of Petitioner's treaters, also predated vaccination, and was in fact investigated thoroughly. *Id.*; Ex. 11 at 4 (noting trace pedal edema in a 2012 visit). But lower extremity edema was not necessarily an indicator that a person suffered from a rheumatic disorder. Rose Rep. at 18. This was especially true here, in Dr. Rose's view, since the primary location for Petitioner's edema was on the lateral aspect of Petitioner's ankle, along with the fact that it was pitting and responsive to Lasix. *Id.* In Dr. Rose's clinical experience, obese individuals[9] can experience lower extremity edema due to chronic venous insufficiency (assuming renal or cardiac causes are ruled out). *Id.* As for Petitioner's joint pain, skin rashes, and high blood pressure, the medical record revealed that all of these symptoms also predated vaccination. *Id.*

Lastly, Dr. Rose discussed vaccine causality as set forth in Dr. Zizic's report. Rose Rep. at 23. As a general matter, Dr. Rose opined that the absence of a credibly-diagnosed injury, as well as the obscurity of symptoms onset post-vaccination, made vaccine causality unlikely. *Id.* He also proposed that Dr. Zizic's report fell short in providing a coherent theory that would explain how an episode of angioedema in close proximity to vaccination could evolve into spondyloarthropathy approximately one and one-half years later. *Id.* at 26. In addition, Dr. Rose questioned the purported relationship between having an underlying autoimmune disease and suffering an abnormal response to the flu vaccine as it has been suggested in Petitioner's case, since it was not understood in the medical field that individuals with rheumatic diseases faced risk from this kind of vaccination. *Id.* at 24. Indeed, this possibility had been investigated but rejected in patients with established autoimmune disease diagnoses, like systemic lupus. *Id.*

C. *Dr. Robert S. Fuijinami*

Dr. Fujinami prepared one report for Respondent addressing certain points raised in Dr. Zizic's expert report. Report, dated May 13, 2019, filed as Ex. C (ECF No. 35-1) ("Fujinami Rep."). Specifically, Dr. Fujinami opined that the flu vaccine could not have caused Petitioner's symptoms, and he also commented on the immune-mediated mechanisms proposed by Dr. Zizic as to causation and how they related to Petitioner's case. Fujinami Rep. at 5-6.

Dr. Fujinami received a Ph.D. from Northwestern University in Immunology-Microbiology. Ex. D at 1. He received post-doctoral training at The Scripps Research Institute where he advanced to Assistant Professor investigating how viruses or infections could induce autoimmune disease. Fujinami Rep. at 1. Currently, Dr. Fujinami is a Professor in the Department of Pathology, Division of Immunology, at the University of Utah School of Medicine. Ex. D at 1.

[9] Certain record evidence suggests Petitioner was characterized by certain treaters as obese when she complained of such lower extremity edema. *See e.g.*, Ex. 2 at 4 (on exam, Petitioner was "obese; tired-looking; tearful"); Ex. 2 at 11 (on exam, Petitioner was "obese; tired-looking").

He is also an Adjunct Professor in the Department of Neurology at the University of Utah School of Medicine. *Id.* Dr. Fujinami wrote one of the most important articles on molecular mimicry[10] regularly cited by petitioners in the Vaccine Program, after his mentor, Dr. Michael Oldstone, popularized the concept.

Dr. Fujinami began his report by addressing the lack of biological plausibility possessed by Dr. Zizic's proposed injury mechanisms. Dr. Zizic had proposed that Petitioner likely developed some form of autoinflammation/autoimmune disease attributable to vaccine-induced activation of the innate immune system in a genetically susceptible individual. Zizic Rep. at 15. But Dr. Fujinami questioned whether any of Dr. Zizic's three mechanisms merited any weight in this case. *Id.*; Fujinami Rep. at 2.

First, Dr. Zizic's "microbial non-self" theory was inapplicable under the circumstances because the flu vaccine contains no products or molecules derived from gram-negative or gram-positive bacteria. Fujinami Rep. at 1. As a result, bacterial cell wall products implicated by this particular mechanism could not have prompted an aberrant immune response for Ms. Camacho Keja. *Id.* at 2. Second, immune system activation attributable to "recognition of missing self" also could not have prompted an autoimmune response due to receipt of the flu vaccine. As Dr. Fujinami explained, "natural killer cells" triggered in the innate immune response are nonspecific, and thus attack infected cells regardless of whether the cells express MHC molecules. *Id.* at 3. Moreover, the flu vaccine itself is not known to decrease levels of MHC molecules on the surface of cells, and may in fact actually increase MHC class I and class II expression (thus further reducing the likelihood this kind of aberrant response could occur after vaccination). *Id.*

Third, Dr. Zizic's proposed "recognition of induced self" mechanism, in which markers of abnormal self that are induced upon infection and cellular transformation are detected and attacked, does not, in Dr. Fujinami's view, provide a credible explanation for how autoimmune disease occurs. As he explained with the example of a wild flu virus infection, the body has the ability to respond to an infectious process by employing phagocytic cells in an innate response to clean up cell debris. Fujinami Rep. at 3. Thus, in response to an ongoing infectious process, affected cells die, releasing their contents into the body, and that debris is in turn cleaned up by phagocytic cells. But the result of this process is not the development of an autoimmune disease—and were it otherwise, millions of individuals infected with influenza virus would go on to develop autoimmune disease. The impact of a vaccine would be no different, Dr. Fujinami noted, observing that unlike a wild virus, nothing in the flu vaccine can replicate in cells or cause tumors. *Id.*

Dr. Fujinami also addressed Dr. Zizic's discussion of "unchecked T-cell and/or B-cell

[10] *See* R. Fujinami et al., *Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease,* 19 Clinical Microbiology Rev. 80–81 (2006).

reactivity to self-antigens" as a driver of autoimmunity, deeming it irrelevant to this case. Fujinami Rep. at 3 (discussing Zizic Rep. at 16). There is no corroborative proof from this record, he maintained, that would suggest Petitioner ever experienced unchecked T and/or B cells responses, given the extensive clinical work ups and lab tests she underwent. *Id.* Had this been occurring, the many physicians who treated Ms. Camacho Keja would most certainly have observed symptoms reflective of such a process (i.e., inflammation or biomarkers suggestive of it) and recorded it in the records. *Id.* at 3-4. Yet, as Dr. Zizic agreed in his own report, test results indicated Petitioner "had negative ANA, ENA, antiphospholipid antibody panel" and "negative autoimmune tests." *Id.* at 4; Zizic Rep. at 8.

Dr. Fujinami also questioned Dr. Zizic's theory that genetic polymorphisms in ERAP1 and ERAP2 could have played a role in the pathogenesis of the autoimmune disease Petitioner is alleged to have experienced. Fujinami Rep. at 4. As Dr. Fujinami understood it, Dr. Zizic seemed to be hypothesizing that viral proteins present in the flu vaccine can *themselves* be improperly processed due to these genetic variants, thereby going on to cause the kind of joint inflammation common to Petitioner's alleged spondyloarthropathy. *Id.* But, Dr. Fujinami deemed this as not biologically plausible, because it mischaracterized the understood way in which the body responds to vaccination. *Id.* Further, there have been no published reports demonstrating that proteins from influenza virus can induce an autoimmune response as a result of ERAP1 and ERAP2 polymorphisms. *Id.*

Finally, Dr. Fujinami discussed how the timing from vaccination to what evidence arguably established the existence of some clinical disease in this case did not support vaccine causality. Fujinami Rep. at 4. Dr. Zizic maintained that Petitioner developed autoinflammation resulting in spondyloarthropathy beginning within 24 hours of vaccination. Zizic Rep. 21-22. But this timeframe was too short, given what is known about immune response to vaccination. Fujinami Rep. at 4. The cell-mediated and humoral immune responses that are involved in autoimmune disease pathogenesis need time to propagate/develop and cause disease following induction. *Id.* at 5. In support, Dr. Fujinami cited three animal studies in which an experimental autoimmune disease was induced by injecting peptides or proteins from myelin with powerful adjuvants. *Id.* Under the best of circumstances, animals such as mice immunized in this manner developed clinical signs of disease after a week. *Id.* (citing A. Abbas et al., *Cellular and Molecular Immunology*, Elsevier Saunders, Philadelphia, PA (2015); M. Cusick et al., *Human T cell expansion and experimental autoimmune encephalomyelitis inhibited by Lenaldekar, a small molecule discovered in a zebrafish screen*, 244 J. Neuroimmunol. 35-44 (2012); J. Libbey et al., *The effects of diet on the severity of central nervous system disease: One part of lab-to-lab variability*, 32 Nutrition 877-883 (2016)). The flu vaccine could not likely have induced autoimmunity in a fraction of that same timeframe. *Id.*

III. Procedural History

This case was initiated in October of 2017. On June 22, 2018, Respondent filed a Rule 4(c) Report stating, *inter alia*, that after review of the petition the case was not appropriate for compensation under the terms of the Act. ECF No. 23. On June 25, 2018, Special Master Millman ordered that Petitioner file an expert report and supporting documents by August 24, 2018. *See* Docket Entry, dated June 25, 2018. On August 20, 2018, Petitioner filed a Motion for Extension of Time to File Petitioner's Expert Report, which was granted. ECF No. 24. On September 21, 2019, Petitioner filed the expert report of Dr. Zizic along with supporting documentation. ECF No. 28-29.

On October 22, 2018, Respondent filed a status report requesting that Petitioner file additional records. ECF No. 30. Respondent's informal motion for production was granted, and Petitioner was ordered to file the requested documents by December 6, 2018. ECF No. 31. On November 19, 2018 Petitioner filed the requested records or submitted affidavits in respect thereto as to why the records were unavailable. ECF No. 32.

On March 14, 2019, Respondent filed Dr. Rose's expert report and supporting documentation. ECF No. 33. Respondent also requested additional time to file an additional expert report. ECF No. 34. On May 13, 2019, Respondent filed Dr. Fujinami's expert report and supporting documentation. ECF No. 35. Petitioner opted not to file supplement expert reports. On June 5, 2019, this case was reassigned to Special Master Daniel Horner. On March 30, 2020, Petitioner submitted a Consent to Change Attorney of Record, which was granted. ECF No. 39.

On July 29, 2020, this case was reassigned to me. ECF No. 40. A status conference was held on August 4, 2020 in which I instructed the parties to file a Joint Status Report on or before 8/21/2020 regarding their preferred means of case resolution (ruling on the record or hearing), and if the latter, proposing two mutually-acceptable days between January 1, 2021 and March 31, 2021 for hearing. *See* Scheduling Order, dated August 4, 2020. In reaction, on August 17, 2020, the parties filed a Joint Status Report indicating a desire for a ruling on entitlement on the current record. ECF No. 42. On August 18, 2020, I set deadlines for briefing. *See* Scheduling Order, dated Aug. 18, 2020. On September 30, 2020, Petitioner formally moved for a Ruling on the Record and filed a supporting brief. ECF No. 43. After an extension of time, Respondent filed his response to Petitioner's motion. ECF No. 47. The matter is now fully briefed and ripe for resolution.

IV. Parties' Arguments

Petitioner asserts that she suffers from a diagnosed injury lasting at least six months after receiving the influenza vaccination on October 17, 2014. Mot. at 15. Petitioner acknowledges that her various symptoms have resulted in multiple speculative medical theories to explain her specific

injury. *Id.* Nonetheless, Petitioner argues that her treater's speculations, plus Dr. Zizic's review and research, preponderantly establish that she suffers from a rheumatological disease known as spondyloarthropathy. *Id.* at 16. Petitioner further argues that her spondyloarthropathy was caused by her 2014 flu vaccine. *Id.* According to Petitioner's expert, Dr. Zizic, the flu vaccine can cause spondyloarthropathy in predisposed individuals through alterations in peptide processing. *Id.* at 18-19. Petitioner points to her development of immediate symptoms such as rash, facial edema, pain, and weight gain as supportive of a cause and effect relationship between the flu vaccine and her injury and differentiates the similar symptoms Petitioner suffered prior to vaccination, which she claims were acute or attributable to pregnancy. *Id.* at 20. Finally, Petitioner argues in the alternative that if I were to find that she suffered from spondyloarthropathy as a pre-existing condition, the flu vaccine significantly aggravated the condition. *Id.* at 23.

Respondent, in contrast, argues that Petitioner has not preponderantly established that she suffers from an inflammatory arthritis, however specified, or that the flu vaccine caused her alleged injury. Opp. at 23. Respondent cites medical records establishing that Petitioner's symptoms pre-date vaccination, as well as Petitioner's consistently-negative rheumatology testing as support. *Id.* In addition, Respondent highlights that spondyloarthropathy was only considered as a "possible differential diagnosis" two and a half years after vaccination, but was never confirmed by treaters. *Id.* at 24 (citing Ex. 3 at 53). Next, Respondent argues that Petitioner's theory of causation is unreliable and unsupported by the medical literature. *Id.* According to Respondent, 24 hours is much too soon for an adaptive autoimmune response to manifest as clinical disease, as Dr. Zizic opines. *Id.* at 29. Further, Petitioner has failed to explain how vaccination causes that process to begin in the first place. *Id.* at 30. Finally, Respondent argues that Petitioner has not established significant aggravation of a preexisting condition because she has provided no relevant theory and her pre-existing condition appears to be lymph node related rather than arthritic. *Id.* at 32.

V. Applicable Law

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006). In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance

of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Services*, 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d 1367, 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury.

The Federal Circuit has consistently rejected the contention that the first *Althen* prong can be satisfied merely by establishing a proposed causal theory's scientific or medical *plausibility*.

See Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." (citing *Moberly*, 592 F.3d at 1322)). Rather, this prong (like the other two) requires a preponderant showing. This naturally flows from the overarching fact that Program petitioners *always* have the ultimate burden of establishing their claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between

the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Significant Aggravation Claims*

Besides arguing that the flu vaccine directly caused her injuries, Petitioner's brief proposes that the same vaccine may have significantly aggravated a preexisting, if mild, autoimmune disorder. Mot. at 23. Where a petitioner so alleges, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *See generally Loving v. Sec'y of Health & Hum. Servs*., 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims combined the *Althen* test with the test from *Whitecotton v. Sec'y of Health & Hum. Services*, 81 F.3d 1099, 1107 (Fed. Cir. 1996), which related to on-Table significant aggravation cases. The resultant "significant aggravation" test has six components, which require establishing:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144; *see also W.C.*, 704 F.3d at 1357 (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). In effect, the last three prongs of the Loving test correspond to the three *Althen* prongs.

In *Sharpe v. Sec'y of Health & Hum. Servs.,* 964 F.3d 1072 (Fed. Cir. 2020), the Federal Circuit further elaborated on the *Loving* framework. Under prong (3) of the *Loving* test, a petitioner need not demonstrate an *expected* outcome, but merely that her current-post vaccination condition is worse than pre-vaccination. *Sharpe*, 964 F.3d at 1081. And a claimant may make out a prima

facie case of significant aggravation overall without eliminating an associated alternative cause of her significantly aggravated injury (although the Circuit did not alter the ability of Respondent to so prove after the burden shifts). *Id.* at 1083.

C. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd sub nom. Rickett v. Sec'y of Health & Hum. Servs.*, 468 F. Appx. 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially

where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Dep't of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

There are, however, situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *Lalonde v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

D. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs*., 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed.

Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

A special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Hum. Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (citing *Brooke Group Ltd.*

v. Brown & Williamson Tobacco Corp., 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")). Expert opinions that fail to address or are at odds with contemporaneous medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Hum. Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

E. *Consideration of Medical Literature*

Petitioner has filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

F. *Consideration of Comparable Special Master Decisions*

In reaching a decision in this case, I have taken into account other decisions issued by special masters (including my own) involving similar injuries, vaccines, or circumstances. I also reference some of those cases in this Decision, in an effort to establish common themes, as well as demonstrate how such prior determinations impact my thinking on the present case.

There is no error in doing so. It is certainly correct that prior decisions from different cases do not *control* the outcome herein.[11] *Boatmon,* 941 F.3d at 1358–59; *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). Thus, the fact that another special master reasonably determined elsewhere, on the basis of facts not in evidence in this case, that preponderant evidence supported the conclusion that vaccine X caused petitioner's injury Y does not compel me to reach the same conclusion in *this* case. Different actions present different background medical histories, different experts, and different items of medical literature, and therefore can reasonably result in contrary determinations.

[11] By contrast, Federal Circuit rulings concerning legal issues are generally binding on special masters in all cases. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). Special masters are also bound within a specific case by determinations made by judges of the Court of Federal Claims after a motion for review is resolved.

However, it is *equally* the case that special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs.,* 76 Fed. Cl. 328, 338–39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions. This is especially so given that special masters not only routinely hear from the same experts in comparable cases but are also repeatedly offered the *same* items of medical literature regarding certain common causation theories. It defies reason and logic to obligate special masters to "reinvent the wheel", so to speak, in each new case before them, paying no heed at all to how their colleagues past and present have addressed similar causation theories or fact patterns. It is for this reason that prior decisions can have high persuasive value—and why special masters often explain how a new determination relates to such past decisions.[12] Even if the Federal Circuit does not *require* special masters to distinguish other relevant cases (*Boatmon,* 941 F.3d at 1358), it is still *wise* to do so.

G. *Evaluation of Expert Credentials and Professional Competence*

It is common in Program cases for special masters to evaluate competing expert opinions when deciding non-Table claims—and that process can be very difficult when the experts are equally well-credentialed and qualified to provide the opinion offered. Under such circumstances, resolution of a claimant's success in establishing causation turns on the comparative reliability of the scientific/medical contentions each side makes, rather than a measure of each particular expert's baseline qualifications against the other. *See, e.g., D'Tiole v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *20 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (determination that causation theory was unreliable did not arise from adequacy of Petitioner's expert, who was expressly deemed well-qualified to provide the opinion given), *mot. for review den'd,* 132 Fed. Cl. 421 (2017), *aff'd*, 726 F. App'x 809 (Fed. Cir. 2018).

In other circumstances, however, weighing the probative value of an expert's opinion fairly takes into account that same expert's qualifications or professional experience. This is most obviously necessary when an expert offers an opinion that plainly exceeds his training or individual competence. *Domeny v. Sec'y of Health & Hum. Servs.,* No. 94-1086V, 1999 WL

[12] Consideration of prior determinations is a two-way street that does not only inure to the benefit of one party. Thus, I would likely take into account the numerous decisions finding no association between vaccination and autism when confronted with a new claim asserting autism as an injury and have informed such claimants early in the life of their case that the claim was not viable for just that reason. But I would *also* deem a non-Table claim asserting GBS after receipt of the flu vaccine as not requiring extensive proof on *Althen* prong one "can cause" matters, for the simple reason that the Program has repeatedly litigated the issue in favor of petitioners.

199059, at * 15 (Fed. Cl. Spec. Mstr. Mar. 15, 1999) (dentist not qualified to offer diagnostic opinion on whether petitioner had experienced a neuropathy), *mot. for review den'd,* slip op., May 25, 1999 (Fed. Cl.), *aff'd*, 232 F.3d 912 (Fed. Cir. 2000). But it can even be an issue with experts who possess immense and impressive credentials, and who in prior cases may have offered reliable opinions. *See, e.g.*, *Rolshoven v. Sec'y of Health & Hum. Servs.,* No. 14-439V, 2018 WL 1124737, at *21 (Fed. Cl. Spec. Mstr. Jan. 11, 2018) (otherwise-competent expert with significant Vaccine Program undermined his credibility in part with constant commentary about relevant legal standards to be applied in case).

H. *Determining Entitlement Via Ruling on the Record*

In accordance with the parties' agreement and my own assessment of how to best decide this case, I am resolving Petitioner's claim on the papers rather than via hearing. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs.,* No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Hum. Servs*., 38 Fed. Cl. 397, 402–03 (1997) (determining that special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417; *Murphy v. Sec'y of Health & Hum. Servs.*, No. 90-882V, 1991 WL 71500, at *2 (Fed. Cl. Spec. Mstr. Apr. 19, 1991).

ANALYSIS

I. The Record Does Not Support Spondyloarthropathy as Petitioner's Injury

It is well-recognized by Program precedent that determining the existence of an alleged injury is often a necessary preliminary step to conducting the *Althen* analysis—for there can be no vaccine injury claim without proof of injury. *Broekelschen*, 618 F.3d at 1346. Here, such an analysis is required to evaluate the nature of Petitioner's post-vaccination condition—and, in particular, whether it factually lines up with her own contentions or her expert's opinion.

Petitioner specifically alleges that the flu vaccine caused her to develop some kind of spondyloarthropathy (*See, e.g.*, Br. at 19). The spondyloarthropathies ("SpAs") are a family of degenerative inflammatory joint disorders, include AS, reactive arthritis, and psoriatic arthritis. *Dorland's Illustrated Medical Dictionary* 1754 (33rd ed. 2020) ("*Dorland's*"). AS (which Dr. Zizic seemed at times to embrace as a possible specific diagnosis for Petitioner) is specifically

"characterized by inflammatory back pain, restricted spinal mobility, peripheral arthritis, enthesitis, and uveitis." *P.S. v. Sec'y of Health & Hum. Servs.*, No. 16-834V, 2020 WL 5351333, at *20 (Fed. Cl. Spec. Mstr. May 15, 2020).

Petitioner has not, however, established that she in fact suffers from a spondyloarthropathy. First, no treater ever so diagnosed her. At best, treaters included that diagnosis in their differentials as a possibility, although it was never definitively embraced, and also proposed it well after vaccination, but without adequate explanation for how her overall clinical picture made it a reasonable diagnosis. *See, e.g.*, Ex. 3 at 53 (spondyloarthropathy proposed in April 2017—more than two years post-vaccination). Indeed, Petitioner's treating physicians appear to have struggled to determine *any* diagnosis for her constellation of symptoms, and their assessments appear in some cases to have been based on Petitioner's self-reported history. *See, e.g.*, Ex. 2 at 106 (Petitioner reported to her treated on December 4, 2014 "that the first time she received the seasonal flu vaccine was last year [2013]."); Ex. 2 at 108 (On December 4, 2014, Petitioner's treater noted, "[t]his is a very complicated case"); Ex. 3 at 53 ("[a]t this point [April 18, 2017], I am starting to wonder if the inflammatory arthritis that she has is related to some form of underlying spondyloarthropathy especially with this new [foot] rash…"). Their speculation never coalesced in any meaningful way into a record-supported diagnosis that would frame the nature of her claimed injury.

Second, the alleged diagnosis lacks preponderant record support. Testing performed on Petitioner consistently *did not display* the biomarkers, specific symptoms, or kinds of inflammation associated with an autoimmune arthritic condition. Rose Rep. at 18-20. In addition, while the record does establish that Petitioner experienced a wide variety of post-vaccination symptoms, and that treaters often speculated about possible diagnostic explanations for them, they are not specific for any kind of spondyloarthropathy. Nothing about Petitioner's persistent lymph node issues or edema have a clear association with some kind of inflammatory arthritic condition, nor has Petitioner shown otherwise. Rather, Petitioner's joint swelling and edema on ultrasound was subcutaneous—hence not related to joint inflammation. *Id.* at 22, 23 (subcutaneous edema is "not a component of the clinical findings in spondyloarthropathies"); Ex. 3 at 96. And the record better supports weight-related chronic venous insufficiency as a cause of Petitioner's edema, given its nature and location. Rose Rep. at 18-19.

At times in his report, Dr. Zizic seems to have favored AS for the SpA variant Ms. Camacho Keja possessed, and tied it to one of his proposed mechanisms. *See* Zizic Rep. at 19, 21 (deeming it "biologically plausible that influenza vaccination in the genetically susceptible host, with specific polymorphisms in ERAP1 and/or ERAP2 could result in altered peptide processing with the generation of arthritogenic peptides resulting in ankylosing spondylitis (spondyloarthropathy)"). But there is no record evidence Petitioner possessed the particular

biomarker most associated with it. The HLA-B27 biomarker[13] is found present in about 80–95 percent of patients with AS, although it is also present in six percent of the general U.S. population (and less than five percent of Caucasians who are positive for the biomarker also have an SpA). As a result, although a positive test for HLA-B27 alone is not diagnostic of AS, its absence is credible evidence *against* the diagnosis. *Godfrey v. Sec'y of Health & Hum. Servs.*, No. 10-565V, 2015 WL 10710961, at *2–3 (Fed. Cl. Spec. Mstr. Oct. 27, 2015), *mot. for review denied*, slip op., Apr. 29, 2016 (ECF No. 109).

But in Petitioner's case, lab testing for *any* rheumatic biomarkers was consistently negative. *See, e.g.*, Ex. 2 at 162 (after analysis of repeat blood work, Petitioner's rheumatology consult explained on April 28, 2015 that Petitioner lacked the diagnostic criteria that would suggest the existence of an autoimmune rheumatic process); Ex. 2 at 202 (August 4, 2015 visit with Dr. Surapaneni); Ex. 3 at 97 ("no ultrasound evidence of inflammatory arthritis"); Rose Rep. at 19-20 (Dr. Rose explaining that higher CRP levels are normal in persons with a high BMI, like Petitioner). And there is nothing in the record indicating that Petitioner ever tested positive for HLA-B27—or that treaters ever thought such testing was in fact warranted.

Finally, other evidence that would support a diagnosis like AS or some other form of spondyloarthropathy is missing from this record. For example, radiographic evidence of changes in the sacroiliac joint is considered a diagnostic criterion for AS. *P.S.*, 2020 WL 5351333, at *20. But as pointed out by Dr. Rose in his expert report and discussed above, Petitioner underwent a CT scan of the abdomen and pelvis on October 27, 2015, which showed no abnormalities. Ex. 2 at 228. And Petitioner's osseous structures revealed no changes. Rose Rep. at 15. As Dr. Rose persuasively proposed, such findings allowed the reasonable inference that there was no fluid on the hip or involvement of the sacroiliac joints at this time. *Id.*

At best, Petitioner's self-reported medical history and affidavits as well as the medical record following the 2014 flu vaccination suggest that she may have suffered from a transient, serum sickness-like reaction[14] to the flu vaccine.[15] Although there is no record evidence to corroborate her contention, and no diagnosis of reactive arthritis either, Petitioner reports having had a similar reaction after her receipt of the flu vaccine in 2013, describing "nonspecific

[13] HLA-B27 is a genetic marker showing susceptibility to conditions such as ankylosing spondylitis. *See Godfrey v. Sec'y of Health & Hum. Servs.,* No. 10-565V, 2015 WL 10710961, at *5 (Fed. Cl. Spec. Mstr. Oct. 27, 2015), mot. for review denied, slip op., Apr. 29, 2016 (ECF No. 109).

[14] Serum sickness in association with vaccination can manifest with symptoms such as joint pain, edema, and fever. *Dorland's* at 1678.

[15] *See Hock v. Sec.'y of Health & Hum. Servs.*, No. 17-168V, 2020 WL 6392770, at *25 (Fed. Cl. Spec. Mstr. Sept. 30, 2020) (petitioner did not preponderantly establish he had rheumatoid arthritis beginning a day after vaccination; his symptoms were instead far more consistent with a transient, reactive arthritis brought on by serum sickness that, even if vaccine-induced, resolved within two months).

symptoms including fatigue, mild fever or rash, [and] arthralgias after flu shot." Ex. 2 at 202. And after a consideration of Petitioner's history, treater Dr. Surapaneni "wondered" if she had in fact experienced a serum sickness or serum sickness-like reaction to vaccination. *Id.* But this putative reaction has not been preponderantly established to be associated with any of Petitioner's *other* symptoms or to be the precursor for a spondyloarthritis, and I conclude from the record that if serum sickness occurred, it likely resolved well short of the six-month period required to establish severity in Program cases. *See* Section 11(c)(1)(D); *Watts v. Sec'y of Health & Hum. Servs.*, No. 17-1494V, 2019 WL 4741748 at *3 (Fed. Cl. Spec. Mstr. Aug. 13, 2019).

As a result of the above, Petitioner's inability to establish she in fact suffered from a spondyloarthropathy as alleged (and as relied upon in her causation theory) is fatal overall to her claim.

II. Petitioner Has Not Carried her Burden of Proof

In addition to not substantiating her alleged injury with preponderant evidence, Petitioner has not met her *Althen* burden.

First, the "can cause" element of the *Althen* test was not satisfied by Dr. Zizic's opinion. As discussed above, Dr. Zizic's proposed mechanisms for how the flu vaccine might propagate an autoimmune disease were, as noted by Respondent in his brief, a "mismatch of immunological concepts and research that have no bearing on explaining alleged vaccination causation specifically in this case." Opp. at 25. Thus, as Dr. Fujinami persuasively demonstrated, these mechanisms were speculative or did not fully align with what is known by medical science about how the immune system actually responds to vaccines. Arguments about the possibility of a misprocessing of vaccine-containing proteins, for example, due to a genetic variant/mutation were insufficiently linked to vaccination (and it was not even demonstrated that Ms. Camacho Keja *possessed* that variant in the first place). In addition, Petitioner offered little in the way of persuasive evidence linking the flu vaccine to *any* form of spondyloarthropathy, beyond case reports (which inherently receive less weight)[16] involving reactive arthritis. Dr. Zizic's vouching for the concept did not gain heft from any demonstrated expertise with rheumatologic diseases he possesses.

The second *Althen* prong (which looks for evidence that the vaccine at issue actually caused the alleged injury, consistent with the proposed causal theory) has similarly not been satisfied. As discussed above, much of Petitioner's post-vaccination symptomology predated vaccination or is not associated with SpA specifically. A year before the vaccination in question, Petitioner was seen on December 6, 2013 for *lymphadenitis* by her primary care physician and by otolaryngology on December 17, 2013. Ex. 2 at 38-39, 101. There was no reference to her

[16] *See Campbell,* 97 Fed.Cl. at 668 (case reports "do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value.").

2013 flu shot (the occurrence of which is based entirely on Petitioner's report) or any wider issues proposed. *Id.* Then, after her October 17, 2014 flu vaccination, on October 27, 2014, Petitioner's primary care provider noted: "[P]atient is now worried about the constellation of [symptoms] she is having that have been ongoing for the last 6 mo[nths] at least…" Ex. 2 at 31. Her skin conditions were also longstanding and did not develop after vaccination. Ex. 2 at 150 ("the rash comes and goes for years now"); 156 (ulcerating rash that had been present since childhood, as well as eczema on her right plantar foot that had been present for about two years). No showing was made to associate these kinds of symptoms with either the flu vaccine or the development of a subsequent spondyloarthropathy.

There is also insufficient evidence of a systemic reaction to vaccination. The main alleged presenting injury at Petitioner's first medical visit after her 2014 vaccination was localized swelling of her "left submandibular node (2 cm in size, firm, tender, mobile)," a common ailment of Petitioner pre-vaccination. Ex. 2 at 33. The assessment was: "Lymphadenopathy." *Id.* at 34. While this is comparable to her alleged 2013 reaction, it is not consistent with the theory that the flu vaccine caused her to experience SpA. The next day, on October 28, 2014, Petitioner went to York Hospital emergency department with the following history: "38-year-old female presents with left calf pain, facial swelling. Symptoms off-and-on for two weeks. Did have some swelling prior to getting flu shot." Ex. 43 at 2. Petitioner also reported a previous similar reaction to a 2013 flu shot and her symptoms subsided after a 5-day course of Prednisone. *Id.* This close-in-time reaction Petitioner asserts was the result of the flu shot however, appears to have subsided relatively quickly. Exam records show that by a November 4, 2014 visit, Petitioner had +1 pedal edema (Ex. 2 at 28) and by December 3, 2014 only "trace pedal edema" was noted. Ex. 2 at 25.

The evidence in this case does not preponderate in support of the conclusion that Petitioner's symptoms only began after her October 17, 2014 vaccination. The most probable explanation is that Petitioner's issues long predated the vaccinations at issue in this case. Thus, the flu vaccine could not have caused them.

Finally, Petitioner cannot demonstrate that the flu vaccine can cause the symptoms Petitioner experienced *within 24 hours* of vaccination. Dr. Zizic's theory, to work, depends on a finding that the immediate, innate response to vaccination would drive a pathologic condition in Petitioner leading to her purported spondyloarthropathy. Zizic Rep. at 21. The adaptive arm of the immune response could not be the primary force for the proposed disease process, as Dr. Fujinami established, since it inherently takes longer for the secondary production of B cells or T cells implicated in that segment of an immune reaction. Fujinami Rep. at 4-6. Dr. Zizic fully agreed (although in so doing he purported to characterize SpA as having less to do with an adaptive response, despite its chronic character). Zizic Rep. at 19 ("[t]he lack of classic autoimmune features leads to the hypothesis that adaptive immune responses are not of primary importance in SpA").

However, even if inflammation related to the innate immune response is clinically relevant to spondyloarthropathy, Dr. Zizic failed to explain *how* vaccination causes this process to begin in the first place, and then how it could evolve into those symptoms construed as spondyloarthritic in nature. Rather, Dr. Zizic speculated that it was the downstream effects of vaccination, where the vaccine somehow causes the "generation of arthritogenic peptides" that result in disease. Zizic Rep. at 21. Again, such contentions were conclusory, scientifically unreliable, and/or not corroborated by the actual medical record. Based on that record and the lack of explanation and support for Dr. Zizic's theory, it is more likely than not that Petitioner experienced at most a transient reaction to the flu vaccine rather than the beginning of a spondyloarthropathy.

III. Petitioner's Significant Aggravation Claim Lacks Preponderant Support

Petitioner's Motion for a Ruling on the Record proposes a significant aggravation claim as an alternative basis for entitlement, based on the contention that her pre-vaccination symptoms reflected an underlying, nascent spondyloarthropathy that the vaccine worsened. Mot at 23-25. But Petitioner has failed to carry her burden of proving by a preponderance of the evidence that the *Loving* prongs are all met, given the medical record in this case as well as deficiencies in Petitioner's causation theory previously discussed.

An immediate obstacle to succeeding on a significant aggravation claim in this case, as Dr. Rose observed, is the fact that Petitioner's pre-vaccination health issues seem to have been dominated by symptoms distinguishable from her claimed injury. The record shows that before October 2014, Petitioner had numerous medical complaints associated with her lymph nodes, not rheumatic-like arthritic inflammation. Rose Rep. at 10. Thus, on August 30, 2010, Ms. Camacho Keja was seen by an ENT specialist from York ENT Associates for submental swelling since late April of that year which had been worsening in the previous weeks. *Id.* (citing Ex. 18). An indirect laryngoscopy was negative and a biopsy of the node was obtained revealing "reactive adenitis." *Id.* Her submental lymphadenitis recurred at the end of 2013, this time preceded by a sore throat. *Id.* at 11.

Then, on October 21, 2014 (eight days after vaccination), Petitioner was seen by her primary care physician with complaints of a solitary skin lesion of concern located on the left side of her chin, with an assessment of "[a]cute lymphadenitis on exam." Ex. 2 at 33. Six days later, Petitioner had a follow-up visit in which the record notes Petitioner had some "generalized lymphandenopathy" a few days after receiving her flu vaccine," but which was responsive to prednisone. *Id.* at 38. This record also notes that Petitioner "was now worried about the constellation of [symptoms] she is having that have been ongoing for the last 6 mo[nths] at least and also with this new lymph node." *Id.*

Such a symptoms timeline does not support a finding that the flu vaccine triggered a noticeable worsening of a pre-existing SpA. Rather, the records indicate that Petitioner was

already experiencing worsening for some time prior to her 2014 vaccination – and in association with lymph-related issues that have not in this case credibly been linked to SpA. She therefore cannot preponderantly establish that the tempo of worsening so increased post-vaccination that the third *Loving* prong is met.[17] At best, the post-vaccination reaction was merely equivalent to the transient reaction Petitioner reported after her 2013 vaccination (assuming for sake of argument that the record in its present form better established both the 2013 vaccination and Petitioner's purported reaction). It otherwise has not been preponderantly demonstrated, as discussed above, that Petitioner *had* any form of spondyloarthropathy pre-2014 vaccination that could have been worsened.

Moreover, even if (under the liberalized version of *Loving* that the Federal Circuit seems to have embraced in *Sharpe*) I conclude generally that *overall* Ms. Camacho Keja was "worse" after her 2014 vaccination (based simply on the fact that she had more reported symptoms thereafter) such that the first three *Loving* prongs are deemed to have been met, prongs four to six (which correspond to the three *Althen* prongs) have not been satisfied, for the reasons already stated. In particular, insufficient preponderant evidence suggests that the flu vaccine *could* worsen spondyloarthropathy, or that it did so in this case. Petitioner has not linked any transient, lymph node-oriented issues that she might have experienced after her vaccination with her purported spondyloarthropathy. Thus, after a thorough review of the medical records and filings, Petitioner has not preponderantly proven that any underlying condition she suffered from, however characterized, was significantly aggravated by the 2014 flu vaccine.

Conclusion

Despite being unable to offer a persuasive theory on causation, Petitioner's claim has some evidentiary basis. She may have suffered from some type of transient vaccine reaction, and her overall health has been consistently problematic, prompting her reasonably to seek treatment. Treaters clearly struggled to define the nature of her condition, and some ultimately speculated that she could have some form of spondyloarthropathy. But she was never diagnosed with the injuries she claims to have been vaccine caused, the record does not support her preferred diagnosis, and her expert's theory was not persuasive or sufficiently supported by independent reliable scientific or medical evidence. As a result, I am compelled to DISMISS the claim.

[17] In reaching this conclusion, I am *not* considering if Petitioner has shown that her overall course is comparatively worse than what an average case of SpA would look like. Rather, I am observing, after record review, that the evidence does not establish that her post-vaccination state was so much different from pre-vaccination to meet the requirements of the third *Loving* prong—especially since her symptoms have not even been associated with spondyloarthropathy in the first place. *See, e.g.*, Ex. 2 at 33 (Petitioner's primary complaint to her primary provider (Dr. Desi) on October 21, 2014, four days after vaccination, was lymph-node related, a condition for which petitioner had extensive workup in the past; On October 27, 2014, lymphadenopathy was again the primary complaint, and at that time, petitioner reported a "constellation of [symptoms] … that have been ongoing for the last 6 mo[nths] at least."

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk **SHALL ENTER JUDGMENT** in accordance with this decision.[18]

IT IS SO ORDERED.

s/Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[18] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.